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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/630,359	07/30/2003	Kamal Bouarab	16721-0220 (42528-288278)	8935
23370	7590	03/11/2005	EXAMINER	
JOHN S. PRATT, ESQ KILPATRICK STOCKTON, LLP 1100 PEACHTREE STREET ATLANTA, GA 30309			FERNANDEZ, SUSAN EMILY	
			ART UNIT	PAPER NUMBER
			1651	

DATE MAILED: 03/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/630,359

Applicant(s)

BOUARAB ET AL.

Examiner

Susan E. Fernandez

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-4 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☒ None of:
- 1) ☒ Certified copies of the priority documents have been received.
  - 2) ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |  |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)            |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>5/28/04</u> . | 6) <input type="checkbox"/> Other: ____  |

### DETAILED ACTION

The preliminary amendment filed June 18, 2004, has been received and entered.

Claims 1-4 are pending and examined on the merits.

#### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3 and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 recites a method wherein "the red alga is stimulated by an extract of the green alga..." It is not clear whether this step is in addition to the steps given in claim 1. Is the extract of the green alga the "elicitor" recited in step (a) of claim 1? Claim 3 recites "**the** green alga", though no green alga is recited in claim 1.

Additionally, the terms "cold" and "hot" render claim 3 indefinite because these terms are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degrees, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear which temperature ranges would be encompassed by "cold conditions" and "hot conditions".

Finally, the phrase "the green alga ground in liquid nitrogen" renders claim 3 indefinite because it is not clear what the phrase defines. Prior to aqueous extraction, had the green alga been pulverized while in liquid nitrogen? The phrase is confusing and difficult to interpret.

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Similarly, claim 4 is rendered indefinite because of inclusion of the phrase “red alga ground in liquid nitrogen.”

Thus claims 3 and 4 are rejected under 35 U.S.C. 112, second paragraph.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Ahern et al. (Biotechnology and Bioengineering, 1983, 25: 1057-1070) or Kessler et al. (U.S. Pat. 5,552,307).

Ahern et al. discloses the extraction of free polyunsaturated fatty acids, including arachidonic acid, from red alga *Porphyridium cruentum*. During cell culture growth, various lipids such as palmitic, stearic, and oleic acids may be added (see “Induced lipogenesis”, bottom of page 1059). Thus these lipids serve as “elicitors” which result in algal production of polyunsaturated fatty acids and their oxidation metabolites. Prior to extraction, culture solutions are stored under nitrogen and ground shelled seeds of *Idesia polycarpa maxim* may be added to culture solutions (page 1060, “Extraction procedure”). The shelled seeds can be defined as an “elicitor”. Seeds comprise peptides, lipids, and/or saccharides. Extraction of fatty acids is accomplished using pentane first, followed by extraction with a solution of

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methanol:benzene:H<sub>2</sub>SO<sub>4</sub>. Moreover, the oxidation metabolites of the extracted fatty acids would have also been extracted.

Kessler et al. discloses using modified proteins as elicitors to increase production of free polyunsaturated fatty acids (such as arachidonic acid) in *Porphyridium cruentum* (column 5, lines 36-40). To determine the presence of the unsaturated fatty acids, those acid would necessarily have been extracted.

A holding of anticipation is therefore required.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ahern et al. in light of Campbell et al. and Gerwick et al., and in view of Thepenier et al. (U.S. Pat. No. 5,338,673) and Galland-Irmouli et al. (Journal of Chromatography B, 2000, 739(1): 117-123).

Ahern et al. discloses the extraction of free polyunsaturated fatty acids, including arachidonic acid, from red alga *Porphyridium cruentum*. During cell culture growth, various lipids such as palmitic, stearic, and oleic acids may be added (see "Induced lipogenesis", bottom of page 1059). Thus these lipids may serve as "elicitors" which result in algal production of polyunsaturated fatty acids and their oxidation metabolites. Prior to extraction, culture solutions are stored under nitrogen and ground shelled seeds of *Idesia polycarpa maxim* may be added to culture solutions (page 1060, "Extraction procedure"). The shelled seeds can be defined as "elicitors". According to Campbell et al., seeds comprise peptides, lipids, and saccharides (pages 740-744, in particular Figure 34.11). Aqueous extraction of fatty acids is accomplished using pentane first, followed by extraction with a solution of methanol:benzene:H<sub>2</sub>SO<sub>4</sub>, which is an organic solvent as it contains benzene. Gerwick et al. states that "many red algae metabolize polyunsaturated fatty acids to oxidized products...", thus the oxidation metabolites of the extracted fatty acids would have also been extracted.

Ahern et al. does not expressly disclose grinding the red algae in liquid nitrogen for extraction of the polyunsaturated fatty acids and the oxidation metabolites.

Thepenier et al. discloses a process for obtaining polyunsaturated fatty acids, including eicosopentaenoic acid and arachidonic acid, from a culture of *Porphyridium cruentum*. A portion of the process is summarized in column 2, lines 50-57. The algae is pulverized or ground prior to extraction with a solvent. This is performed using a homogenizer-grinder (column 4,

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lines 25-33), and the solvent is preferably an organic solvent (column 4, lines 49-51). The use of the homogenizer-grinder requires "an alternative sequence of pressure increases and decreases..."; as well as temperature controlled to remain below 30°C.

Galland-Irmouli et al. discloses a method requiring extraction of a substance, a light-harvesting pigment, from red algae. Red algal cells were lysed by grinding the cells in liquid nitrogen. See abstract.

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to substitute the extraction techniques used in Ahern et al. for those described in Thepenier et al. Furthermore, it would have been obvious to substitute the algal pulverization procedures described in Thepenier et al. with the grinding step described in Galland-Irmouli et al.

One of ordinary skill in the art would have been motivated to do this because Thepenier et al. provides a method that allows for optimization of both algal growth and polyunsaturated lipid production (column 2, lines 18-23). One would have been motivated to freeze and grind the cells in liquid nitrogen rather than using a homogenizer-grinder for pulverization of algal cells because it would have eliminated the need to control pressure and temperature, and therefore the costs entailed with controlling these variables. A holding of obviousness is therefore proper.

Claims 1 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kessler et al. in view of Ahern et al., Gerwick et al., Thepenier et al., and Galland-Irmouli et al.

Kessler et al. does not expressly disclose the aqueous extraction of the polyunsaturated fatty acids and their oxidation metabolites from *P. cruentum* wherein the red algae is ground in liquid nitrogen for extraction of the polyunsaturated fatty acids and the oxidation metabolites.

As discussed above, Ahern et al. discloses the extraction of free polyunsaturated fatty acids, including arachidonic acid, from *P. cruentum*. More specifically, it discloses fatty acid extraction accomplished by extraction with pentane, followed by extraction with a solution of methanol:benzene:H<sub>2</sub>SO<sub>4</sub>, which is an organic solvent as it contains benzene.

Additionally, Gerwick et al. discloses that “many red algae metabolize polyunsaturated fatty acids to oxidized products...”

Thepenier et al. discloses a process for obtaining polyunsaturated fatty acids, including eicosopentaenoic acid and arachidonic acid, from a culture of *Porphyridium cruentum*. A portion of the process is summarized in column 2, lines 50-57. The algae is pulverized or ground prior to extraction with a solvent. This is performed using a homogenizer-grinder (column 4, lines 25-33), and the solvent is preferably an organic solvent (column 4, lines 49-51). The use of the homogenizer-grinder requires “an alternative sequence of pressure increases and decreases...”, as well as temperature controlled to remain below 30°C.

Galland-Irmouli et al. discloses a method requiring extraction of a substance, a light-harvesting pigment, from red algae. Red algal cells were lysed by grinding the cells in liquid nitrogen. See abstract.

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to apply the extraction methods disclosed in Ahern et al. to the *P. cruentum* culture stimulated by modified proteins disclosed in Kessler et al. Also, it would have been obvious that



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the oxidation metabolites of the extracted fatty acids would have also been extracted when using the Ahern extraction procedures. It would have been obvious to substitute the extraction techniques used in Ahern et al. for those described in Thepenier et al. Finally, it would have been obvious to substitute the algal pulverization procedures described in Thepenier et al. with the grinding step described in Galland-Irmouli et al.

One of ordinary skill in the art would have been motivated to do this because Kessler et al. states that fatty acids from *P. cruentum* such as arachidonic acid are “useful metabolites” (column 5, line 37). Therefore, one would have been motivated to isolate them from the algal culture. There would have been a reasonable expectation of success that the extraction techniques used in Ahern et al. to isolate the polyunsaturated fatty acids and their oxidation metabolites from algal culture would have performed equally as well when applied to a culture stimulated with modified proteins. Moreover, one would have been motivated to apply techniques used in Thepenier, et al. because Thepenier et al. provides a method that allows for optimization of both algal growth and polyunsaturated lipid production (column 2, lines 18-23). One would have been motivated to freeze and grind the cells in liquid nitrogen rather than using a homogenizer-grinder for pulverization of algal cells because it would have eliminated the need to control pressure and temperature, and therefore the costs entailed with controlling these variables. A holding of obviousness is therefore proper.

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tasende (Scientia Marina, 2000, 64(4): 421-426) in light of Gerwick et al. and in view of Bouarab et al. (Plant Cell, 1999, 11(9): 1635-1650).

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Tasende discloses the extraction of various free polyunsaturated fatty acids, including arachidonic acid, from *Chondrus crispus*. See Table 2 on page 423. Gerwick et al. states that “many red algae metabolize polyunsaturated fatty acids to oxidized products...”, thus the oxidation metabolites of the extracted fatty acids would have also been extracted.

Tasende does not expressly disclose stimulation of red alga with any elicitor.

Bouarab et al. discloses that “the green alga *Acrochaete operculata* is a primary invasive organism of *C. crispus*” (page 1636, first column, third paragraph).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to conclude that *A. operculata* had served as an elicitor for production of polyunsaturated fatty acids and their oxidation metabolites in the Tasende study.

One of ordinary skill in the art would have been motivated to conclude this because the artisan would have concluded that the algal samples collected in the Tasende study would have contained *A. operculata*. Since Tasende showed that extraction of polyunsaturated fatty acids was possible from these samples, it would have been obvious that *A. operculata* had served as an “elicitor”. A holding of obviousness is therefore proper.

Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tasende, Gerwick et al., and Bouarab et al. as applied to claims 1-2, and further in view of Bouarab et al.

As discussed above, claims 1 and 2 are disclosed in Tasende, Gerwick et al., and Bouarab et al.

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These references do not teach stimulating the red alga with an extract of a green alga which had been obtained by aqueous extraction under cold or hot conditions applied to green alga which had been ground in liquid nitrogen.

Bouarab et al. teaches grinding *A. operculata* cells in liquid nitrogen. The ground *A. operculata* is resuspended in a buffer. The resuspension step can be defined as "aqueous extraction". See page 1647, second column, second paragraph.

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to add a solution of *A. operculata* in buffer to the red algal samples used in the Tasende study.

One of ordinary skill in the art would have been motivated to do this because it would have ensured that all red algal cells in the Tasende study would have been in contact with an extract of *A. operculata*. Otherwise, there would not have been any guarantee that each and every algae cell had been in contact with any component of *A. operculata*. Addition of an extract of *A. operculata* would have allowed for a more sound scientific study by eliminating one factor of potential variability. A holding of obviousness is therefore proper.

Claims 1, 2, and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tasende, Gerwick et al., and Bouarab et al. as applied to claims 1-2 above, and further in view of Nakano et al. (Plant Science (Limerick), 1995, 104(2): 127-133).

As discussed above, claims 1 and 2 are disclosed in Tasende, Gerwick, and Bouarab et al. Tasende et al. discloses drying algal samples by performing lyophilization, followed by pulverization of the samples (page 422, first column, fourth paragraph). A series of aqueous

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extraction steps follow, using ether, an organic solvent, repeatedly, as well as extraction with hexane (page 422, first column, last paragraph, through second column, first paragraph).

Tasende et al. does not expressly disclose grinding the red algae in liquid nitrogen for extraction of the polyunsaturated fatty acids and their oxidation metabolites.

Nakano et al. discloses extraction of catalase from a red algae. Nakano et al. states that “extraction from frozen and powdered material under liquid nitrogen was more efficient than that from fresh or freeze-dried material” (abstract).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have frozen the algal cells under liquid nitrogen rather than freeze-drying the cells by lyophilization.

One of ordinary skill in the art would have been motivated to do this because there is a reasonable expectation of success that the conclusion drawn in the Nakano study would have also been true for extraction of lipids in the Tasende study. A holding of obviousness is therefore proper.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan E. Fernandez whose telephone number is (571) 272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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